FILE 'HOME' ENTERED AT 14:33:52 ON 08 MAR 2006

=> file reg

=>

Uploading C:\Program Files\Stnexp\Queries\10528179.str

chain nodes : 17 18 19 20 21 22 23 24 25 26 27 28 29 ring nodes : 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 30 31 32 chain bonds : 7-11 8-18 9-30 14-17 18-19 19-20 20-21 20-27 21-22 22-23 22-28 23-24 24-25 24-29 25-26 ring bonds : 1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-10 7-8 8-9 9-10 11-12 11-16 12-13 13-14 14-15 15-16 30-31 30-32 31-32 exact/norm bonds : 20-27 22-28 24-25 24-29 25-26 30-31 30-32 31-32 exact bonds : 7-11 8-18 9-30 14-17 18-19 19-20 20-21 21-22 22-23 23-24 normalized bonds : 1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-10 7-8 8-9 9-10 11-12 11-16 12-13 13-14 14-15 15-16

#### Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:CLASS 18:CLASS 19:CLASS 20:CLASS 21:CLASS 22:CLASS 23:CLASS 24:CLASS 25:CLASS 26:CLASS 27:CLASS 28:CLASS 29:CLASS 30:Atom 31:Atom 32:Atom

## L1 STRUCTURE UPLOADED

=> d l1

L1 HAS NO ANSWERS

L1 STI

Structure attributes must be viewed using STN Express query preparation.

```
=> s l1 full
             24 SEA SSS FUL L1
=> file ca
=> s 13
            32 L3
=> s liquid chromatograph?
        651439 LIQUID
        394430 CHROMATOGRAPH?
        83200 LIQUID CHROMATOGRAPH?
L5
                 (LIQUID (W) CHROMATOGRAPH?)
=> s 14 and 15
            4 L4 AND L5
L6
=> s 14 and resolv?
        178031 RESOLV?
L7
             3 L4 AND RESOLV?
=> s 16 or 17
            6 L6 OR L7
```

=> d ibib abs fhitstr 1-6

COPTRIGHT 2006 ACS on STN
141:395429 CA
Method for producing ethyl
copyl4-(4-fluorophenyl)quinolin-3-yl]-3,5-dihydroxy-6-A ANSWER 1 OF 6 ACCESSION NUMBER: TITLE: (3R,5S,6E)-7-[2-cyclops 4 (4-fluorophenyl)quinolin-3-yl]-3,5-dihydroxy-(heptenoate Onishi, Atsushi; Tachibana, Kozo Daicel Chemical Industries, Ltd., Japan; Nissan Chemical Industries, Ltd., Japan; Nissan Chemical Industries, Ltd., PCT Int. Appl., 28 pp. CODEN: PIXXD2
Patent
Japanese INVENTOR(S): PATENT ASSIGNEE(S): SOURCE: DOCUMENT TYPE: LANGUAGE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION: APPLICATION NO. DATE' PATENT NO. KIND DATE 20040423 BZ, CA. CH, PI. GB. GD, KR. KZ, LC, MZ, NA, NI, SK, SL, SY, ZA. ZM, ZM ZM, AM, AZ, DE, DK, EE, RO, SE, SI, MR, NE, SN, BY, ES, KP, MX, SG, YU, ZM, CZ, PT, ML, R: CH, DE, PR, GB, IT, LI, IE PRIORITY APPLN. INFO.: BP 2004-729193 JP 2003-119807 A 20030424 W 20040423 WO 2004-JP5894 Disclosed is a method for producing Et (3R,55,6E)-7-[2-cyclopropyl-4-(4-fluorophenyl)quinolin-3-yl]-3,5-dihydroxy-6-heptenoate (1) from a AB cion containing a mixture of optical isomers of Et (6E)-7-[2-cyclopropyl-4-(4-fluorophenyl)quinoline-3-yl]-3,5-dihydroxy-6-heptanoate by means of the liquid chromatog, using a packing material having a carrier and, carried thereon, a polysaccharide derivative, characterized in that a part or

the hydrogen atoms of the hydroxyl groups and amino groups of the polysaccharide derivative are substituted with one or more substituents,

as a carbamoyl group wherein one hydrogen atom is substituted with an aromatic group having a specific alkyl group. The method allows the price.

production
of the above (3R,5S,6E)-isomer I with enhanced productivity compared to a
conventional method. Thus, 100 g cellulose and 794 g 4-isopropylphenyl
isocyanate were stirred in pyridine at reflux for 60 h to give 84.69
cellulose tris(4-isopropylcarbamate) (II) which (100 g) was dissolved in
600 mL acetone and added to 3-aminopropylated silica gel (400 g),
followed

B ANSWER 2 OF 6 CA COPYRIGHT 2006 ACS on STN

140:287282 CA Purification of a 3,5-dihydroxy-6-heptenoate isomer Yoshimura, Yuji, Yasukawa, Masami; Morikiyo, Syuji; Mateumoto, Hiroo; Takada, Yasutaka; Adachi, Michiaki Niesan Chemical Industries, Ltd., Japan PCT Int. Appl., 29 pp.

COUMENT TYPE: ANGUAGE: English MAILY ACC. NUM. COUNT: 1 ACCESSION NO. TITLE: INVENTOR(S): PATENT ASSIGNEE(S): SOURCE: DOCUMENT TYPE: LANGUAGE: PAMILY ACC. NUM. COUNT: PATENT INFORMATION: DATE PATENT NO. KIND DATE APPLICATION NO. DATE

MO 2004026388 AI 20040401 MC 2003-JP11643 20030911
MC 2005-JP11643 MC 2003-JP11643 MC 20030911
MC 2005-JP11643 MC 2003-JP11643 MC 20030911
MC 2005-JP11643 MC 2005-JP11643 MC 20030911
MC 2005-JP11643 MC 2005-JP11643 MC 20030911
MC 2005-JP11643 MC 2005-JP1643 MC 20030911
MC 2005-JP11643 MC 2005-JP11643 MC 2005-JP11643 MC 20030911
MC 2005-JP11643 M PRIORITY APPLN. INFO.: W 20030911 WO 2003-JP11643

OTHER SOURCE(S): MARPAT 140:287282

An alkyl (3R,58)-7-[2-cyclopropyl-4-(4-fluorophenyl)quinolin-3-yl)-3,5-dihydroxy-6-heptenoate I (R = alkyll, which is an intermediate for a cholesterol-reducing agent (s HWG-COA reductase inhibitor), is purified

ANSMER 1 OF 6 CA COPYRIGHT 2006 ACS on STN (Continued) by evapm. of the solvent under reduced pressure to give II-supported c silice gel as a packing material. This packing material was packed in steinless steel column (0.46 cm diam. X 25 cm length) by the slurry

to give a HPLC column. A mixt. of Et (3R,55,6E) - and (3S,5R,6E)-7-[2-cyclopropyl-4-(4-fluorophenyl)quinolin-3-yl]-3,5-dihydroxy-6-heptenoat was sepd. by the HPLC column prepd. above using n-hexane/2-propanol

(50/50

(50/50

vol./vol. ratio) as the eluent at 40°.

17 147003-20-6, Ethyl rel-(3R,5S,6E)-7-[2-Cyclopropyl-4-(4-fluorophenyl)quinolin-3-yll-3,5-dihydroxy-6-heptenoate
RL. PEP (Physical, engineering or chemical process); PPP (Physical)
process); PEOC (Process)
(method for producing Et (3R,5S,6E)-7-[2-cyclopropyl-4-(4-fluorophenyl)quinolin-3-yll-3,5-dihydroxy-6-heptenoate by liquid chromatog, separation using polysaccharide carbamate derivative
supported on
silica gel)
RN 147008-20-6 CA
6-Reptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester, (3R,5S,6E)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry. Double bond geometry as shown.

REFERENCE COUNT: THERE ARE 9 CITED REPERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

ANSWER 2 OF 6 CA COPYRIGHT 2006 ACS on STN liq. chromatog. on Silica gel. 167073-19-0P (Continued)

147073-19-0P
RL: PUR (Purification or recovery); PREP (Preparation)
(purification of a 3,5-dihydroxy-6-heptenoate isomer)
167073-19-0 CA
6-Heptenoic acid, 7-{2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl}-3,5-dihydroxy-, ethyl ester, (3R,5S,6E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

Page 4

```
8 ANSWER 3 OF 6 CA COPYRIGHT 2006 ACS on STN
CCESSION NUMBER: 118:287535 CA
17LE: Process for preparation of optically active
 7-[2-cyclopropy]-4-(4-fluoropheny])quinolin-3-y]-3,5-
dihydroxyhept-6-enoic acid ethyl ester
INVENTOR(S):
Niehino, Shigeyoshi; Matsushita, Akio; Yokoyama,
Shuji; Kawachi; Yasushiro; Sasaki, Hiroshi
PATENT ASSIGNEE(S):
UBE Industries, Ltd., Japan
PCT Int. Appl., 26 pp.
CODEN: PIXXD2

DOCUMENT TYPE:
LANGUAGE:
Japanese
FAMILY ACC. NUM. COUNT:
PATENT INTOPMATION:
1
   DOCUMENT TYPE:
LANGUAGE:
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
                                                                                                                                                                                                            APPLICATION NO. DATE

**MO 2002-JP9638 20020919
BA, BB, BB, BR, BY, BZ, CA, CH, CN, DZ, EC, EE, ES, FI, GB, GD, GE, GH, MF, KE, LC, LK, LR, MK, ND, MN, NC, MZ, ND, NZ, CM, PH, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, ZA, ZM, ZM, SK, LT, TM, TM, TR, TT, TZ, TM, TM, TT, UB, BG, CH, CY, CZ, DE, DK, EE, ES, MC, NL, PT, SE, SK, TR, BP, BJ, CP, HL, MR, NE, SN, TD, TU

JF 2001-284633 20010919

JF 2001-284633 A 20010919
                             PATENT NO.
                                                                                                                                  KIND
                                                                                                                                                                  DATE
MO 2003037073

M: AE, AG, AL,
CO, CR, CU,
GM, HR, HU,
LS, LT, LU,
PL, PT, RO,
UA, UG, US,
RM: GH, GM, KE,
KG, KZ, MD,
PJ, FR, GB,
CG, CI, CM,
JP 2005255522
JP 2005255523
PRIORITY APPLN: INPO::
                                                                                                                           A1 20030403

AM, AT, AU, A2,

C2, DE, DK, DM,

ID, IL, IN, S,

IV, MA, MD, MG,

IV, SQ, SE, SG,

UZ, VC, VN, YU,

IS, MM, MZ, SD,

RU, TJ, TM, AT,

GR, IE, IT, LU,

GA, GN, GO, GM,

A2 20050922
                                                                                                                                                                                                                               JP 2001-284634
                 This invention pertains to prepn method of (3R,SS)-7-[2-cyclopropyl-4-{4-fluorophenyl)quinolin-3-yl]-3,5-dihydroxyhept-6-enoic acid Et ester
                          ul
as an intermediate for an HMG-CoA reductase inhibitor (cholesterol-
lowering agent) in high yield by reacting an amine salt of
(3R, SS)-7-[2-cyclopropyl-4-(4-fluorophenyl)quinolin-3-yl]-3,5-
dihydroxyhept-6-enoic acid with an alc. in a solvent in the presence of
                          acid, or by a method comprising reacting the salt with an esterifying agent in a solvent in the presence of a base. For example, 7-(2-cyclopropy)-4-(4-fluoropheny))quinolin-3-y-1)-3,5-dihydroxyhept-6-enoic acid was reacted with PhCM2NN2 in AcORt to obtain 7-(2-cyclopropy)-4-(4-fluoropheny))quinolin-3-y-1)-3,5-dihydroxyhept-6-enoic acid benzylamine salt (94.9%). The above salt was resolved
 enoic acid densylamine sait (94.5%). The above sait was reactived
with THF to give
(3R,5S)-7-[2-cyclopropy14-(4-fluorophenyl)quinolin-3-yl}-
3,5-dihydroxyhept-6-enoic acid benzylamine sait (60.0%, 99.1% ee, 99.8%
del. The above optically active sait was reacted with EtOH in the
presence of concentrated aqueous HCl to afford
(3R,5S)-7-[2-cyclopropy1-4-(4-
fluorophenyl)quinolin-3-yl}-3,5-dihydroxyhept-6-enoic acid Et ester
 L8 ANSWER 4 OF 6 CA
ACCESSION NUMBER:
137:384764 CA
Process for producing (3R,55)-7-substituted-3,5-dihydroxyhept-6-enoic acid
INVENTOR(S):
Niehino, Shigeyoehi; Yokoyama, Shuji; Kawachi, Yasuhiro; Saeski, Hiroshi
PATENT ASSIGNEE(S):
Ube Industries, Ltd., Japan
PCT Int. Appl., 33 pp.
CODEN: PIXXD2
PATENT INFORMATION:
PATENT INFORMATION:
1 Japanese
   DOCUMENT TYPE:
LANGUAGE:
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
PATENT INFORMATION:

PATENT NO. KIND DATE

NO 2002092570

W: AE, AG, AL, AM, AT, AU, AZ

CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GB, GH,

GM, HR, HI, ID, II, IN, AS, JP, KE, KG, KP, KR, KZ, LC, LK, LK,

LS, LT, LU, LV, MA, MED MG, NK, MN, MM, MK, MX, NO, NZ, OM, PH,

PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,

UA, UG, US, UZ, VN, YU, ZA, ZM, ZM, AM, AZ, BY, KO, KZ, OM, PH,

RN: GH, GM, KE, LS, MM, MZ, SD, SL, SZ, TZ, UG, ZM, ZM, AT, BE, CH,

CY, DE, DK, ES, PI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,

BF, BJ, CP, CG, CI, CM, GA, GM, GG, GM, ML, MR, NE, SN, TD, TO

JP 2005047803

A2 20050224

JP 2001-145358

A 20010515
```

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

Disclosed is a process for producing a (3R,5S)-7-(2-cyclopropyl-4-(4-fluorophenyl)quinolin-3-yl]-3,5-dihydroxyhept-6-enoic acid represented by the formula (I) which comprises optically resolving with an achiral amine compound a mixture of optical isomers of a -cyclopropyl-4-(4-fluorophenyl)quinolin-3-yl]-3,5-dihydroxyhept-6-enoic acid represented by the formula (II). The optical resolution involves contacting II with an achiral amine to form II achiral amine salt, recrystg. the salt to form I achiral amine salt, recrystg. the salt to form I achiral amine salt, recryst.

an acid to give I. This process does not use expensive chiral amines and is suitable for industrial preparation of I which is an intermediate for

anticholesteremic agent (HMG-CoA reductase inhibitor). Thus, 4.21 g II (preparation given), 1.07 g benzylamine, and 30 mL EtOAc were added to a

flask and cooled to 0° with stirring, upon which crystals precipitated
The precipitated crystals were filtered, washed with StCAc cooled at 0°,
and dried under reduced pressure to give 94.9% II benzylamine selt. II
benzylamine selt (4.22 g) and 84 mL THF were added to a 100 mL flask,
warmed to 50° with attring to give a homogeneous solution, and cooled
to 0°, upon which crystals precipitated The precipitated crystals were

RI: IMP (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation) (process for preparation of optically active 7-[2-cyclopropyl-4-[4-fluorophenyl]ouinolin-3-yl]-3,5-dihydroxyhept-6-enoic acid Et ester) 173336-32-2 CA (Selegian of the control of

ANSWER 3 OF 6 CA COPYRIGHT 2006 ACS on STN (Continued) (1009), which was crystd. from (1-Pr)20 and heptane to produce cryst.sample (91.0%, 99.9% ee, 99.8% de). 173336-12-2P

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP

Absolute stereochemistry. Rotation (+). Double bond geometry unknown.

THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

LB

ANSWER 4 OF 6 CA COPYRIGHT 2006 ACS on STN (Continued) and washed with 42 mL THF cooled at 0°. This procedure was repeated twice to give 2.53 g 1 benzyl amine salt (60.04) which (2.11 g) and 10 mL MeOH were added to a 50 mL flask, adjusted to pH 3.5 by adding

1

M aq. HCl, and extd. with 10 mL EtOAc twice, followed by drying the EtOAc ext. over anhyd. MgSO4 and concn. to give 1.66 g I (99.04).

IT 475445-78-4P, 7-[2-cyclopropy]-4-(4-fluorophenyl]quinolin-3-yl)-3,5-dihydroxyhept-6-enoic acid impropyl ester Ri: RCT (Reactant): SPN (Synthetic preparation): PREP (Preparation): RACT (Reactant or reagent)

(preparation of (3R.SS)-7-[2-cyclopropy]-4-(4-fluorophenyl)-quinolin-3-yl]-3,5-dihydroxyhept-6-enoic acid by optical resolution using achiral amine

via formation of achiral amine salt, recrystn., and treatment with acid)

acid)
475645-78-4 CA
6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, 1-methylethyl ester (9CI) (CA INDEX NAME)

REFERENCE COUNT:

THERE ARE 6 CITED REPERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

Page 5

OTHER SOURCE(S):

L8 ANSWER 5 OF 6 CA COPTRIGHT 2006 ACS on STM ACCESSION NUMBER: 116:325435 CA Process for producing optically active ethyl (3R,5S,6B)-7-[2-cyclopropyl-4-(4-[luorophenyl]quinolin3-yl]-3,5-dihydroxy-6-heptenoate
Onishi, Atsushi; Muraxumi, Koichi; Tachibana, Kozo
Daicel Chemical Industries, Ltd., Japan; Nissan
Chemical Industries, Ltd., Japan; Nissan
Chemical Industries, Ltd., Japan; Nissan
Chemical Industries, Ltd.
CODEN: PIXED2

DOCUMENT TYPE:
DATENT INFORMATION:
1

2 parest INFORMATION:
1 DOCUMENT TYPE: LANGUAGE: PAMILY ACC. NUM. COUNT: PATENT INFORMATION: US 6946557 PRIORITY APPLN. INFO.: A 20001013 The process for producing an optically active isomer of Et 7-[2-cyclopropyl-4-(4-fluorophenyl)quinolin-3-yl)-3,5-dihydroxy-6-heptenoate comprises optically resolving, at a high efficiency, a mixture of optical isomers of the compound, characterized in that a packing comprising a support and cellulose tris(4-chlorophenylcarbamate) nited thereon in a specific proportion is used to chromatog. isolate the target isomer under such conditions as to result in a specific retention volume The title compound is an intermediate for the known hypolipemic NK 104. 121661-131-0 IT 121661-13-0
RL: ANT (Analyte): ANST (Analytical study)
(process for producing optically active Et
(3R.SS.6E)-7-[2-cyclopropyl4-(4-fluorophenyl)quinolin-3-yl]-3,5-dihydroxy-6-heptenoate)
RN 121661-13-0 CA
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester (9CI) (CA INDEX NAME) L8 ANSMER 6 OP 6
ACCESSION NUMBER:
130:316585 CA
TITLE:
Chiral separation of a pharmaceutical intermediate by a simulated moving bed process
AUTHOR(S):
NAMENTE SOURCE:
SOURCE:
SOURCE:
Journal of Chromatography, A (1999), 832(1 + 2), AUTHOR(S): CORPORATE SOURCE: SOURCE: 55-65 55-65

CODEN: JCRAEY; ISSN: 0021-9673

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The chiral separation of a pharmaceutical intermediate by a simulated LANGUAGE:

AB The chiral separation of a pharmaceutical intermediate by a simulated moving bed (SMB) system on a pilot-scale is described. The operating conditions were chosen from results simulated by the software, help, developed by Novasep, based upon data from a single column. The productivity of the SMB system is tested by the separation of an ester of quinoline mevalonic acid at various internal flow-rates. The eluent consumption is also discussed.

The step time to switch the ports to enter or withdraw solns. is one of important factors influencing the productivity.

In 12166:1-13-0P, DOLE RL: ANT (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses) (chiral separation of pharmaceutical intermediate by simulated moving bed process)
12166:13-0 CA
6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester (9CI) (CA INDEX NAME)

THERE ARE 15 CITED REFERENCES AVAILABLE FOR

RECORD. ALL CITATIONS AVAILABLE IN THE RE

L8 ANSWER 5 OF 6 CA COPYRIGHT 2006 ACS on STN (Continued)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

PORMAT

REFERENCE COUNT: THIS

FORMAT

=> s 14 not 18

L9 26 L4 NOT L8

=> d ibib abs fhitstr 1-26

L9 ANSWER 1 OP 26 CA
ACCESSION NUMBER:
1171E: 143:139169 CA
PREPARENT ASSIGNEE(S): Observed to the control of t DOCUMENT TYPE: LANGUAGE: PAMILY ACC. NUM. COUNT: PATENT INFORMATION: PATENT NO. APPLICATION NO. MO 2005063711 A1 20050714

W: AE, AG, AL, AM, AJ, AU, AZ, CN, CO, CR, CU, CL, DE, DK, GE, GH, GM, HR, HJ, DI, LL, LK, LR, LS, LT, LL LV, MA, MO, NZ, CM, EQ, GM, KE, LS, LM, MZ, AZ, BY, KG, KZ, MD, RU, TJ, EE, ES, FI, FR, GB, GR, HU, RO, SE, SI, SK, TR, BF, BJ, MR, NE, SN, TD, TG

PRIORITY APPLA. INFO.: MO 2004-JP1951 20041217
BA. BB, BG, BR, BM, BY, BZ, CA, CH, TH, DZ, EC, EE, EG, ES, FI, GB, GD, M, IE, JP, KE, KG, KP, KR, KZ, LC, MD, MG, MK, MN, MM, MX, MZ, NA, NI, RO, RU, SC, SD, SE, SG, SK, SL, SY, UG, US, UZ, VC, VN, YU, ZA, ZM, ZM, MA, SD, SL, SZ, TZ, UG, ZM, ZM, AM, TM, AT, BE, BG, CH, CY, CZ, DE, DK, TH, AT, BE, BG, CH, CY, CZ, DE, DK, TH, ST, TT, LT, LU, MC, ML, PL, PT, CF, CG, CI, CM, GA, GN, GQ, GM, ML, JP 2003-431788 A method for producing a drug substance of crystalline pitavastatin um excellent in stability, is presented. In the production of a compound (pitavastatin calcium) the water content is adjusted to a level of 5-15%, and the crystal form is controlled to be crystal form A, thereby to

in
the drug excellent in stability.
167073-19-0
RE: RCT (Reactant); RACT (Reactant or reagent)
(preparation of crystal form of pitavastatin calcium)
167073-19-0
CA
6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5dihydroxy-, ethyl ester, (3R,5S,6E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

L9 ANSWER 2 OF 26 CA COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 142:481922 CA
AUTHOR(S): ORANGA KEZUPA; Ueda, Makoto
CORPORATE SOURCE: API Business Division, API Corporation Japan
SOURCE: CODEN: SPCHEY; ISSN: 0262-2662
DMG WOrld Media (uk) Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB An enzyme expressed in a recombinant microorganism annionism activity for the preparation of Pitavastatin Et ester by diastereoselective reduction the
3-keto-5-hydroxy and double enantioselective reduction of the 3,5-diketo

r
precursors.
167073-19-0P. Pitavastatin ethyl ester
RL: BPN (Biosynthetic preparation); BIOL (Biological study); PREP
(Preparation)
(asym. reduction using biocatalytic reactions)
167073-19-0 CA
6-Heptenoic acid, 7-{2-cyclopropyl-4-{4-fluorophenyl}-3-quinolinyl}-3,5-dihydroxy-, ethyl ester, (3R,5S,6B)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown

REFERENCE COUNT:

THERE ARE 13 CITED REFERENCES AVAILABLE FOR

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 1 OF 26 CA COPYRIGHT 2006 ACS on STN (Continued)

REFERENCE COUNT THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L9 ANSWER 3 OF 26 CA
ACCESSION NUMBER:
117LE:
142:393305 CA
A process for producing high-purity
3,5-6.hydroxy-6-heptenoic acid derivatives, useful as medicinal intermediates
Yoshimure, Yuji; Yasukawa, Masami; Morikiyo, Syuji; Takada, Yasutaka; Matsumoto, Hiroo
Nissan Chemical Industries, Ltd., Japan
PATENT TYPE:
DOCUMENT TYPE:
LANGUAGE:
PANILY ACC. NUM. COUNT:
English
1
PATENT INFORMATION: FAMILY ACC. NUM. COUNT: PATENT INFORMATION: AI 2005 AI 2005 AI AI 20 CV. CZ. DE HA HU. IV. PG. PH. PL. KE, LS. MM. KZ. MD. RU. FR. GB. GR. BF. BJ. CF. PATENT NO. APPLICATION NO. DATE PATENT NO.

MO 2005033083

W: AE, AG, AL,
CN, CO, CR,
GE, GH, GM,
LK, LR, LS,
NO, NZ, OM,
TJ, TM, TM,
RM: BM, GH, GM,
AZ, BY, KG,
EE, ES, FI,
SI, SK, TR,
SN, TD, TG
PRIORITY APPLN: INFO:: APPLICATION NO. LATE

144 WO 2004-JP14289 20040932
AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, LL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, MA, MD, MG, MK, MN, MM, MX, MZ, NA, NI, PT, RO, RU, SC, SD, SE, SG, KS, LS, SY, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AW, TJ, TM, AT, BE, BG, CH, CT, CZ, DE, DK, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, CG, CI, CM, GA, GN, GG, GM, ML, MR, NE, JP 2003-346019 OTHER SOURCE(S): MARPAT 142:392305

The invention relates to a process for producing a high-purity 3.5-dihydroxy-6-heptenoic acid derivs. of formula I (R is alkyl) alc.-containing solvent was employed in a process for obtaining an

ically disomer by optical resolution
RI: PUR (Purification or recovery); PREP (Preparation)
(process for producing high-purity 3,5-dihydroxy-6-heptenoic acid

ANSMER 3 OF 26 CA COPYRIGHT 2006 ACS on STN (Continued)
derivs. useful as medicinal intermediates)
121661-13-0 CA
6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5dihydroxy-, ethyl ester (9CI) (CA INDEX NAME)

THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE REFERENCE COUNT:

FORMAT

ANSWER 4 OF 26 CA COPYRIGHT 2006 ACS on STN (Continued)

L9 ANSMER 4 OP 26 CA
ACCESSION NUMEER:
ACCESSION NUMEER:
TITLE:
Crystalline forms of pitavastatin calcium
Van Der Schaaf, Paul Adriean; Blatter, Pritx;
Sselegievicz, Martin; Schoening, Kai-Uwe
Ciba Specialty Chemicala Holding Inc., Switz.
PATENT ASSIGNEE(S):
SOURCE:
DOCUMENT TYPE:
LANGUAGE:
FAMILY ACC. NUM. COUNT:
PATENT INDEMATION: PAMILY ACC. NUM. COUNT: PATENT INFORMATION:

APPLICATION NO. PATENT NO. KIND DATE DATE 

AB The present invention is directed to new crystalline forms of Pitavastatin hemicalcium salt, referred to hereinafter as polymorphic Forms A, B, C,

D,

B and P, as well as the amorphous form. Purthermore, the present invention is directed to processes for the preparation of these crystalline forms and the amorphous form and pharmaceutical compns. comprising these crystalline

calline forms or the amorphous form. The hemicalcium salt was prepared from pitavastatin tert-Bu ester in tert-Bu ether and MeOH, NaOH added, and

phase extracted with Me tert-Bu ether. Then CaCl2 was added to give a form IT A. 586966-54-3

Absolute stereochemistry.
Double bond geometry as shown.

L9 ANSWER 5 OF 26 CA COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 140:41958 CA
Process for the manufacture of organic compounds
STOURCE: STOURCE: STOURCE: STOURCE: CODEN: USXXCO
DOCUMENT TYPE: LANGUAGE: Patent
LANGUAGE: GODEN: USXXCO
PATENT ACC. NUM. COUNT: 1

LANGUAGE: PAMILY ACC. NUM. COUNT: PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE US 2003233001 US 6909003 PRIORITY APPLN. INFO.: 20031218 US 2003-428257 20030502 GB 2002-10234 A 20020503

OTHER SOURCE(S): MARPAT 140:41958

This invention relates to a process for the manufacture of analogs, (3R,5R)-R1(CM2)2CM(OH)CH2CM(OH)CH2CO2H and (3R,5S,6S)-R1CH:CHCH(OH)CH2CO(H)CH2CO2H and (3R,5S,6S)-R1CH:CHCH(OH)CH2CO2H (RIP = cyclic statin analog residue), of known HMG-COA reductase inhibiting statins via an enantioselective

rton
using a ruthenium catalyst. Thus, pitavastatin hemicalcium salt
(3R,5S,6B)-I (R = 1/2Ca1+, X1 = X5 = B-OH-o-H) was prepared via
enantioselective reduction of 3,5-dioxo-ester (6E)-I (R = Et, X3 = X5 =

Catalyzed by

(1R, ZR)-N-p-toluenesulfonyl-1, 2-diphenylethylenediamine-RuIIp-cymene complex in DMF followed by treatment with Bt3N to give
3,5-diol-ester (2R, SS, 6E)-I (R = Et, X3 = X5 - B-OH-a-H) which
was subsequently converted to the target hemicalcium salt.

If 167073-19-0P

RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic
preparation); PREP (Preparation); RACT (Reactant or reagent)
(process for asym. synthesis of analogs of statins via
enantioselective
reduction using a ruthenium catalyst)

RN 167073-19-0 CA
6-Heptenoic acid, 7-{2-cyclopropyl-4-{4-fluorophenyl}-3-quinoliny

6-Heptenoic acid, 7-{2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester, (3R,55,6E)- (9CI) (CA INDEX NAME)

L9 ANSWER 5 OF 26 CA COPYRIGHT 2006 ACS on STN. (Continued)

REFERENCE COUNT:

THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

ANSWER 6 OF 26 CA COPYRIGHT 2006 ACS on STN (Continued) acid, e.g., prepd. from diethyl-3-hydroxyglutaric acid in 3-steps, and

sodium salt of di-Me methylphosphonate afforded claimed chiral

phosphonate
II in 77% yield and 99.1% chiral purity. Of note is the enantioselective esterage mediated hydroylais of diethyl-3-hydroxyglutaric acid in 99.5% chiral purity. The prepn. of the sodium salt of rosuvastatin using

phosphonate II was also provided. The present invention does not have

problem of removing reaction byproducts and the disposal of waste assocd.
with current methodologies.
386946-54-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or resgent)
(intermediate, preparation of rosuvastatin and related HMG-COA

(intermediate; preparation of the distribution of the distribution

Absolute stereochemistry.
Double bond geometry as shown.

REFERENCE COUNT:

FORMAT

THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

L9 ANSMER 6 OP 26 CA COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 139:337984 CA Preparation of rosuvastatin and related HMG-COA reductase inhibitors via a common chiral intermediate Lim, Evang-Min CLS Laboratories, Inc., S. Korea PATENT ASSIGNEE(S): COEN: PIXXO2

DOCUMENT TYPE: PATENT AND COUNT: PATENT AND DOCUMENT TYPE: LANGUAGE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION: PATENT NO. KIND DATE APPLICATION NO. APPLICATION NO. DATE

\*\*MO 2003-KR7707 20030409

\*\*BA, BB, BG, BR, BY, BZ, CA, C.H, CN, DZ, EC, EE, ES, FI, GB, GD, GE, GR, JP, KE, LC, LK, LK, LS, LNN, MM, MX, MZ, NI, NO, NZ, OM, PH, SG, SK, SL, TJ, TM, TN, TT, TT, ZA, ZM, ZM, ZM, ZM, ZM, AM, AZ, BY, BE, BG, CH, CY, CZ, DE, DK, EE, ES, LJJ, MC, NL, PT, RO, SE, SI, SK, TR, GM, GG, GM, ML, MR, NE, SN, TD, TG (MR, 2002-19340)

\*\*RE 2002-19340 A 20020409

\*\*KR 2002-19340 A 20020409 MO 2003095112 A1 20031023
M: AE, AG, AL, AM, AT, AU, AZ,
CO, CR, CU, CZ, DE, DK, DM,
GM, HR, HU, ID, IL, IN, IS,
LT, LU, LV, MA, MD, MG, MK,
FL, PT, RO, RU, SC, SD, SE,
UA, UG, US, UZ, VC, VN, YU,
RM: GM, GM, KE, LS, MM, MZ, SD,
KG, KZ, MD, RU, TJ, TM, AT,
FT, FR, GB, GR, HU, IE, IT,
BF, BJ, CP, CG, CI, CM, GA,
KR 2003106502 A 20031027
PRIORITY APPLN: INFO::

WO 2003-KR707 W 20030409

OTHER SOURCE(S): CASREACT 139:337984; MARPAT 139:337984

 ${\sf AB}-{\sf A}$  process for the preparation of rosuvastatin and related HMG-CoA reductase

inhibitors via the common chiral intermediate I [X = P(=0)R12, S(0)R1; R1 = H, alkyl, aryl; P = OH protecting group, e.g., t-butyldimethylsilyl]

was
disclosed. For example, condensation of Bt tert-Bu
(3R)-3-hydroxyglutaric

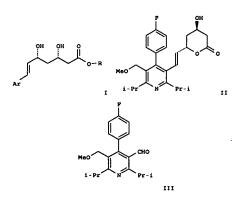
L9 ANSMER 7 OF 26 CA
CCPYRIGHT 2006 ACS on STN
139:323335 CA
139:323335 CA
139:323335 CA
139:323335 CA
139:323335 CA
139:32335 CA
139:323335 CA
149:323335 CA
149:323335 CA
149:3233335 CA
149:323335 CA
149:32335 CA
149:3235 CA
149:3235

DOCUMENT TYPE: LANGUAGE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

APPLICATION NO.

EP 2003-8308
, GR, IT, LI, LU, NL,
, AL, TR, BG, CZ, EE,
DE 2002-10216967
US 2003-413199
JP 2003-112036
DE 2002-10216967 PATENT NO. DATE A1 20031022 DE, DK, ES, PR, LV, PI, RO, MK A 20031113 A1 20031218 A2 20031128 EP 1354865 R: AT, BE, CH, IE, SI, LT, DE 10216967 US 2003232989 JP 2003335756 PRIORITY APPLN. INFO:: 20030410 SE, MC, PT, HU, SK 20020416 20030414 20030416 A 20020416

OTHER SOURCE(S): CASREACT 139:323335; MARPAT 139:323335



Preparation of aromatic aldehydes (Ar-CHO) via ozonolysis of aromatic

ANSMER 7 OF 26 CA COPYRIGHT 2006 ACS on STN (Continued) the corresponding lactone (Ar \* (un)substituted aryl, heteroaryl; R \* H, slkyl, cycloalkyl, etc.] is disclosed. For example, ozonolysis of

lactone  $$\operatorname{II}$$  in methanol afforded aldehyde III in 83% yield. The process is

claimed

useful for the recycling of HMG-CoA reductase inhibitors unwanted, i.e,
false (sic), disastereomers.

IT 147008-20-6

RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of aromatic aldehydes via the ozonolysis of aromatic
alkenes)

RN 147008-20-6 CA

CO 6-Heptenoic ecid. 7-[2-cyclonronyl-4-[4-filenrombent]] 2-mid-Name

6-Heptenoic ecid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester, (3R,5S,6E)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry. Double bond geometry as shown.

REFERENCE COUNT:

THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

PORMAT

ANSMER 8 OF 26 CA COPYRIGHT 2006 ACS on STN (Continued)
Provide a novel carbonyl reductage originating in a microorganism
belonging to the genus Ogatage, an encoding gene, recombinant expression,
and use for producing optically active alcs. By reducing ketones having
general structures I (R = H, alkyl, aryl; R1 = :0, OH, (R)-OH; R2 = OH,
(S)-OH, :0) with the use of carbonyl reductage, optically active alcs.,

particular,
(3R,SS)-(E)-7-[2-cyclopropyl-4-(4-fluorophenyl)-quinolin-3-yl]3,5-dihydroxy-hept-6-enoic acid esters, can be produced. A novel
carbonyl

onyl reductage was isolated from Ogataes minuta var. nonfermentans strain IFO 1473. Its substrate specificity was investigated with various ketones

aldehydes. Its activity for reduction of 2,2,2-Trifluoroacetophenone was significantly inhibited by  ${\rm Hg}(I)$  ion and  ${\rm Zn}(II)$  ion. Its gene was

cloned,
sequenced, and expressed in E. coli. The recombinant enzyme was used in production of.

(3R,5S)-(S)-7-[2-cyclopropyl-4-(4-fluorophenyl)-quinolin-3-yl)3,5-dihydroxy-hept-6-enoic acid Et ester (3R,5S-DOLE) from

(S)-7-[2-cyclopropyl-4-(4-fluorophenyl)-quinolin-3-yl)-3,5-dioxo-hept-6-enoic acid Et ester (DXE) or SS-(S)-7-[2-cyclopropyl-4-(fluorophenyl)-quinolin-3-yl)-5-hydroxy-3-oxohepto-6-enoic acid Et ester (5S-MOLE), is described. The yield was 319 µg (31.9% with 100% e.e. optical purity), and 807 µg (80.7% with 97% e.e. optical purity), resp.

17 167073-19-0P, (3R,5S)-(E)-7-[2-Cyclopropyl-4-(4-fluorophenyl)-quinolin-3-yl)-3,5-dihydroxy-hept-6-enoic acid Ethyl ester RL: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)

(Preparation)

(Preparation)
(Ogataea minuta carbonyl reductase, encoding gene, and use for producing optically active alcs.)
167073-19-0 CA
6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester, (3R,5S,6E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

REPERENCE COUNT:

THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

L9 ANSMER 8 OF 26 CA COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:
139:272910 CA
Ogataea sinuta carbonyl reductase, encoding gene, and
use for producing optically active alcohols
Hiraoka, Hirotoshi; Ueda, Makoto; Hara, Mari
Mitsubishi Chemical Corporation, Japan; Nissan
Chemical Industries, Ltd.
PCT Int. Appl., 54 pp.
COEN: PIXXD2
DOCUMENT TYPE:

Acceptable Accep

DOCUMENT TYPE: LANGUAGE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION: Patent Japanese

	PA:	PENT	NO.			KIN	D	DATE			APPL	ICAT	ION	NO.		D.	ATE	
	MO	2003	0786	34		Al		2003	0925		NO 2	003-	JP32	62		2	0030	318
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								DK,										
								IN.										
								MG,										
								SD,										
								VN.					,					
		RW:						М2,					ug.	ZM.	ZW.	AH.	AZ.	BY.
								TM.										
								IB.										
								CH,										
	CA	2479																
	ΑU	2003	2210	82		A1		2003	0929		AU 2	003 -	2210	82		2	0030	318
		2003																
		1491																
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			IB,	SI,	LT,	LV,	PI,	RO,	MK,	CY,	AL.	TR,	BG,	CZ,	EE,	HU,	5K	
	US	2005	0486	33		A1		2005	0303	- 1	US 2	004-	9432	02		2	0040	917
PRIC	RIT	APP	LN.	INFO	. :						JP 2	002-	7592	1	- 1	A 2	0020	319

WO 2003-JP3262

W 20030318

GI

ANSWER 8 OF 26 CA COPYRIGHT 2006 ACS on STN (Continued)

FORMAT

L9 ANSWER 9 OP 26
ACCESSION NUMBER:
139:214343 CA
Process for the manufacture of HMG-CoA reductase inhibitory mevalonic acid derivatives
Sedelmeier, Gottfried, Mathes, Christian
Novartis A.-G., Switz., Novartis Pharma G.m.b.H.
CODEM: PIXXD2
DOCUMENT TYPE:

CODEM: PIXXD2
DATE:

ACCOMPANT TYPE:

CODEM: PIXXD2
DATE:

ACCOMPANT TYPE:

CODEM: PIXXD2
DATE:

ACCOMPANT TYPE:

CODEM: PIXXD2
DATE:

CODEM: PIXXD2
DA DOCUMENT TYPE: Patent English LANGUAGE: PAMILY ACC. NUM. COUNT: PATENT INFORMATION: PATENT NO. KIND DATE APPLICATION NO. DATE A1 WO 2003-EP1738 20030828 20030220 WO 2003070717 2003070717 A1 20030828 W0 2003-EP1738
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ,
CO, CR, CU, CZ, DE, DK, DM, DZ, BC, BE, ES, FI, GG,
HR, HU, ID, II, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
LV, MA, MD, MX, MO, NX, NO, NZ, OM, PH, PL, PT, RO,
SG, SK, TJ, TM, TN, TR, TT, TT, UA, US, UZ, VC, VV, VV,
RM: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH,
DK, ES, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NIL,
SK, TR

AD 20030828 W0 2003-84713255 20030220
CA. CH. CN,
GD, GE, GH,
LK, LT, LU,
RU, SC, SE,
ZA, ZW
CY, CZ, DE,
PT, SE, SI, SK, TR

CA 2473075

AA 20030823

CA 2003-2477075

AD 2003218994

A1 20030909

AU 2003-218994

A1 20030909

AU 2003-218994

A1 20030909

AU 2003-218994

A1 20030909

AU 2003-218994

AU 2003-2200

AU 2005-22081

AU 2004-22081

AU 2005-22081

AU 2005-22 NO 2004003919 PRIORITY APPLN. INFO.: WO 2003-EP1738 W 20030220 OTHER SOURCE(S): MARPAT 139:214343

Mevalonic acid derivs. I [R = cyclic residue; X = CH2CH2, CH:CH] are prepared by treating R1R2R3P:CHCOCH2CO2R4 [R1-R3 = (un)substituted Ph;

aliphatic, cycloaliph., aromatic] with RCHO, reducing the resulting RCH:CHCOCH2CO2R4 in presence of a chiral metal BINAP or TaDPEN catalyst, treating the resulting alc. with an ester enclate, reducing the second

L9 ANSMER 10 OF 26 CA COPYRIGHT 2006 ACS on STN

139:164712 CA
ASymmetric titanium mediated dimilyloxydiene/aldehyde addition process for the preparation of 5-hydroxy-B-Ketcesters.

INVENTOR(S): Chen, Guang-Pei; Kapa, Prasad Koteswars; Loeser, Eric M.; Beutler, Ulrich; Zaugg, Werner; Girgis, Michael

Novertis A.-G., Switz.; Novertis Pherma G.m.b.H. PCT Int. Appl., 53 pp. CODEN: PIXXD2 Patent English

PATENT ASSIGNEE(S):

DOCUMENT TYPE:

LANGUAGE: PAMILY ACC. NUM. COUNT: PATENT INFORMATION:

DATE APPLICATION NO. PATENT NO. DATE KIND A2 A3 20030807 WO 2003-EP804 20030127 WO 2003064382 WO 2003064382 2003064382 A3 20031211
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LV, MA, MD, MK, NM, MX, NO, NZ, OM, PH, PL, PT, SG, SK, TJ, TM, TN, TR, TT, UA, US, UZ, VC, VN, RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, DK, EE, ES, FI, FR, GB, GR, RU, IE, IT, LU, MC, SK, TR CA, CH, CN, GD, GE, GH, LK, LT, LU, RU, SC, SE, ZA, ZW CY, CZ, DE, PT, SE, SI, BZ, GB, LC, RO, YU, CH, NL, A1 B2 AA A2 20031106 US 2003-350615 US 2003208072 20030124 US 6835838 CA 2472340 20041228 20030807 1472227 BR 2003007236 2005516064 ZA 2004005239 US 2004249154 NO 2004003586 PRIORITY APPLN. INFO.: 20041007 NO 2004-3586 US 2002-352316P 20040827 P 20020128 US 2002-383188P P 20020524 US 2003-350615 A3 20030124

WO 2003-EP804

W 20030127

CASREACT 139:164712: MARPAT 139:164712 OTHER SOURCE(S):

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \* A process for the preparation of I (R1 = (un) substituted (cyclo) alkyl, R2-7 = H, halo, OH, (un) substituted (cyclo) alkyl, aryl, aralkyl, etc.)

analogs is disclosed. The process involves the Ti(OPr-i)4/(S)-BINOL

Page 12

ANSWER 9 OF 26 CA COFFRIGHT 2006 ACS on STN (Continued) group, and hydrolysing the ester group. Thus, CICH2COCH2CO2Et was

Absolute stereochemistry.
Double bond geometry as shown.

REFERENCE COUNT: THIS

THERE ARE 10 CITED REFERENCES AVAILABLE FOR 10

RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

ANSMER 10 OF 26 CA COPYRIGHT 2006 ACS on STN (Continued) mediated addn. of II [R1 = as above; R, R' = alkyl] to III [R2-7 = as above]. Por instance, II [R1 = Et; R, R' = Me] (prepn. given) is reacted with III [R2 = P; R3-7 = H] (HPF, 4Å mol. sieves, (S-BINOL/Ti(OPT-1)4, 19\*, 2 days) to give I [R1 = Et; R2 = P; R3-7 = H] in 81.64 yield (after purifn.) and the amt. of undesired enantioner was below the limit of detection. Addnl. examples demonstrated sidechain manipulation (to the δ(S)-β(R)-ester) and subsequent conversion to pitavestatin (calcium sait) via the intermediacy of the 2H-pyranone. Exptl. details regarding mol. sieve prepn. and their use in a fixed bed reactor are given.

187073-19-0P
RL: INF (Industrial manufacture); RCT (Reactant); SFN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (asym. titenium mediated disilyloxydiene/aldehyde addition process for preparation of δ-hydroxy-β-ketoesters)

6-Heptenoic acid, 7-12-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester, (3R, SS, SE)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown

L9 ANSWER 11 OF 26 CA COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:
118:204870 CA
Processes for preparing calcium salt forms of statins
NVENTOR(S):
Niddam-Hildeshein, Velerie; Lifshitz-Liron, Revital;
Lidor-Hadas, Rami
Pharmaceutical Industries Ltd., Israel; Teva
Pharmaceuticals UEA, Inc.
COUNTER:
DOCUMENT TYPE:
LANGUAGE:
PRINTED
PRINTED
Emplish
PANILY ACC NUM: COUNT:
6 LANGUAGE: PAMILY ACC. NUM. COUNT: PATENT INFORMATION: PATENT NO. KIND DATE APPLICATION NO. DATE PATEST NO. KIND DATE APPLICATION NO. DATE

NO 2003016317 A1 20030727 M0 2002-U326012 20020816

N: AR A, AG, AL, AM, AT, AU, AZ, EA, BB, BG, BR, BY, BZ, CA, CH, CM, CO, CR, CU, CZ, DE, DK, DM, DZ, SC, ER, ES, PI, GB, GD, GE, GH, GM, HR, HU, ID, N, IN, IS, JDP, KR, KG, KP, FR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MM, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SSS-SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, LY, VC, VN, YU, ZA, ZM, ZM

RM: GH, GM, KE, LS, MM, MZ, SD, SL, SZ, TZ, UG, ZM, ZM, ZM, CH, CY, CZ, DB, DK, ES, SS, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CP, CG, CI, CM, GA, GN, GO, GM, ML, NR, NS 6528661 B2 200309524 A1 20020725 US 2001-37412 20011024

US 2003114685 A1 20030217 CA 2002-2450820 20020816

US 6777752 B2 20040817 EP 2002-2450820 20020816

US 6777752 B2 20040817 EP 2002-22556 20020816

US 6777752 B2 20040817 EP 2002-2759374 20020816

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, EP 1425287 A. DR. DK. ES, FR. M. C. PT. 20040619 BP 2002-759374 20020816 RITY APPLN. INFO.:

20040679 BP 2002-759374 20020816 RITY APPLN. INFO.:

20040921 TR 2003-20231 20020815 20020816 A 2004103 CR 2002-85999 20020816 CR 2003-80337 A 2005106 JP 2003-521239 20020816 CR 2003-9373 A 2004103 CR 2003-529913 20020816 CR 2003-80337 A 2004103 CR 2003-529913 20020816 CR 2003-80337 A 20041062 A 2004018 CR 2003-8034 CR 2003-8034 CR 2003-8034 CR 2003-8034 CR 2004018 CR 2003-8034 CR 2004018 CR 2004018 CR 2004018 CR 2004018 CR 2004018 CR 2003-8034 CR 2003-8 US 2005197501 PRIORITY APPLN. INFO.: US 2001-37412 A 20011024 US 2000-249319P P 20001116 US 2001-312144P P 20010813 US 2001-326529P P 20011001 US 2002-222556 A3 20020816

ANSWER 11 OF 26 CA COPYRIGHT 2006 ACS on STN (Continued)

WO 2002-US26012

W 20020816

THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE REFERENCE COUNT:

L9 ANSWER 11 OF 26 CA COPYRIGHT 2006 ACS on STN (Continued)
US 2004-803414 A1 20040318

OTHER SOURCE(S): MARPAT 138:204870

Processes for preparing hemicalcium salts of a statins RCH(OH)CH2CO2H (R = statin organic radical selected from prevastatin, fluvastatin, cerivastatin, atorvastatin, rosuvastatin, pitavastatin, sinvastatin, or lovastatin) from an ester derivative or protected eater derivative of the statin by using calcium hydroxide are provided. The ester or protected ester derivative is contacted with

rium
hydroxide to obtain the calcium salt. Preferred statins are
insatatin,
pitavastatin and atorvastatin, simvastatin and lovastatin. In processes
beginning with a protected satin ester derivative, the protecting group

hydrolyzed during salt formation by contact with calcium hydroxide, or is contacted with an acid catalyst followed by contact with calcium hydroxide. Thus, diol-protected storvastatin ester I (R = CMe3, R3R5 = CMe2) was treated with an 80% aqueous soln of AcON at rt for 20 h to

the deprotected ester I (R = CMe3, R3 = R5 = H) which was in turn dissolved

EtOH, treated with a saturated soln of Ca(OH)2 containing Bu4N+Br- and

EtOH, treated with a saturated soln of Caton, a Communication at 45° for 24 h to give atorvastatin hemicalcium salt I (R = 1/2Cs, R3 = R5 = H) in 77° yield for the two steps.

IT 167073-19-0
RL: RCT (Reactant); RACT (Reactant or resgent) (processes for preparing calcium salt forms of statins)
RL: RCT (Reactant); RACT (Reactant or resgent) (processes for preparing calcium salt forms of statins)
RC 167073-19-0 CN
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester, (3R,55,6E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

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L9 ANSWER 12 OF 26 CA COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 138:106481 CA

Enantioselective addition of diketene to aldehydes promoted by Chiral Schiff base-titanium alkoxide complex. Application to asymmetric synthesis of potential inhibitors of HMG coenzyme reductase Hayashi, Masahiko; Yoshimoto, Kazuya; Hirata,
Nachito;

Tanaka, Kiyoshi; Oguni, Nobuki; Harada, Katsumasa;
Mateushita, Akio; Kawachi, Yasuhiro; Sasaki, Hiroshi
Department of Chemistry, Faculty of Science, Kobe
University, Kobe, 657-8501, Japan

SOURCE: Israel Journal of Chemistry (2002), Volume Date 2001,
41(4), 241-246
CODEN: ISJCAT; ISSN: 0021-2148

LOSEY Pages Publishing
JOURNANT TYPE: Loser Pages Publishing
JOURNANT TYPE: CASPARCT 138:106481

AB Highly enantioselective addition of diketene to aldehydes was achieved by
using novel Schiff base-titanium alkoxide complexes. Up to 92% ee of
5-bydroxy-3-oxo esters was obtained. This procedure provides an
efficient
method for the asym. synthesis of potential inhibitors of the contractions.
     AUTHOR(S):
Nachito;
 5-hydroxy-3-oxo esters was obtained. This procedure provides an efficient method for the asym. synthesis of potential inhibitors of MMG coenzyme reductase. Ligands included 2-(1,1-dimethylethyl)-6-[[(18)-1-(hydroxymethyl)-2-methylpropyl]imino]methyl]phenol (1), 2,4-bis(1,1-dimethylethyl)-6-[1-([(18)-1-(hydroxymethyl)-2-methylpropyl]imino]methyl]phenol, 2,4-bis(1,1-dimethylethyl)-6-[1-([(18)-1-(hydroxymethyl)-2-methylpropyl]imino]methyl]phenol, 2-(1,1-dimethylethyl)-6-[1-([(18)-1-(hydroxymethyl)-2-methylpropyl]imino]methyl]-4-methylphenol (II), etc. For example, the addition of benzaldehyde to diketene in the presence of I and itianium tetrzisopropoxide gave (58)-65-624 yield and in 824 enentiomeric excess. Schiff base II was used as ligand in the reaction of diketene with (28)-3-(2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-2-propenel to give (59,68)-7-(2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl)-5-hydroxy-3-oxo-6-Heptenoic acid Et ester. This product
                                       an intermediate in the synthesis of (4R,6S)-(4R,6S)-6-[(1E)-2-[2-cyclopropy]-4-(4-fluorophenyl)-3-quinolinyl]ethenyl]tetrahydro-4-hydroxy-2H-pyran-2-one (niswastatin).
167073-19-09, (3R,5S,6E)-7-[2-Cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-6-heptenoic acid ethyl ester
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
```

(Reactant or reagent)
(stereoselective addition of diketene to aldehydes promoted by chiral Schiff base-titanium alkoxide complexes)
167073-19-0 CA 167073-19-0 CA
6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5dihydroxy-, ethyl ester, (3R,SS,6E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

L9 ANSWER 12 OF 26 CA COPYRIGHT 2006 ACS on STN (Continued)

REFERENCE COUNT: THERE ARE 16 CITED REPERENCES AVAILABLE FOR RECORD. ALL CITATIONS AVAILABLE IN THE RE

ANSWER 13 OF 26 CA COPYRIGHT 2006 ACS on STN (Continued) alkyl, Ph, an alkali metal ion, or an alk. earth metal ion) with ozone L9

then conducting either redn. of the resulting compd. with an inorg.

or compd. or hydrogenolysis of the resulting compd. Thus, a soln. of 5.0 g Rt (6E)-3,5-dihydroxy-7-{2-cyclopropyl-4-(4-fluorophenyl)quinolin-3-yl]hept-6-enoate in 50 g MeOH was cooled to 0°, followed by introducing 1 g ozone(g) to the soln. at 0-5° over 1 h and removing excess ozone with N. To the resulting soln. was added dropwise a soln.

0.85 g thiourea in 14.1 g H2O at 0.5° over 10 min, stirred at the same temp. for 1 h, treated with 26 g H2O, and stirred at 5° for 1 h to give, after filtering off pptd. crystals ad washing them with 6 g

aq. MeoH, and drying them, 2.81 g I (86.7% yield and 99.2% purity).

1T 477950-34-8

RL: RCT (Reactant); RACT (Reactant or reagent)
(process for preparation of
2-cyclopropyl-4-(4-fluorophenyl)quinoline-3cholesterol-lowering agent)

RN 477950-34-8 CA

CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5dihydroxy-, ethyl ester, (6E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

REPERENCE COUNT:

PORMAT

THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

ANSWER 13 OF 26 CA COPYRIGHT 2006 ACS on STN SSION NUMBER: 138:24649 CA ACCESSION NUMBER: Process for preparation of 2-cyclopropyl-4-(4-fluorophenyl)quinoline-3-carbaldehyde by ozonolysis TITLE: ethyl (68)-3,5-dihydroxy-7-[2-cyclopropyl-4-(4-fluorophenyl)quinolin-3-yl)hept-6-enoate Matsumoto, Hiroo; Shimisu, Takanori Daicel Chenical Industries, Ltd., Japan; Nissan Chemical Industries, Ltd. PCT Int. Appl., 15 pp. CODEN: PIXXO2 Patent Japanese 1 INVENTOR(S): PATENT ASSIGNER(S): SOUTH CTE . DOCUMENT TYPE: PAHILY ACC. NUM. COUNT: PATENT INFORMATION: APPLICATION NO. PATENT NO. KIND DATE DATE M0 2002098859 A1 20021212 M0 2002-JP4712 20020515
M: AB, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CA, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EB, ES, PI, GB, GD, GE, GH, GR, HR, HU, ID, IL, IN, IS, JP, KE, KE, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, NN, MM, MK, MZ, ND, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TM, TR, TT, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZM, AM, AZ, BY, KG, KZ, MD, RU, TJ, JP 2001-208501 A 20010709

of

OTHER SOURCE(S): CASREACT 138:24649; MARPAT 138:24649

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

Described is a process for preparing 2-cyclopropyl-4-(4-fluorophenyl)quinoline-3-carbaldehyde (I) which is important as an intermediate for the synthesis of drugs, i.e. RMG-COA reductase inhibitor for cholesterol-lowering agent, efficiently from an unnecessary antipode, characterized by treating a compound represented by formula (II) or (III) (wherein A is -CHOH- or CO; and R is hydrogen, optionally branched Cl-H

WO 2002-JP4712

W 20020515

```
L9 ANSMER 14 OF 26 CA COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:
137:310823 CA
Method for preparing alkyl 7-quinolinyl-3,5-
dihydroxyhept-6-encete as intermediate for HMG-COA
reductase inhibitor
TOKUNEGAS, Kenichi; Kozawa, Masami; Suzuki, Kenji
Nissan Chemical Industries, Ltd., Japan
PCT Int. Appl., 20 pp.
CODEN: PIXXD3
PATENT TYPE:
LANGUAGE:
PAMILY ACC. NUM. COUNT:
1
  PAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
                PATENT NO.
                                                                                                 DATE
                                                                                                                                       APPLICATION NO
                                                                                                                                                                                                             DATE
               M0 2002081451 A1 20021017 M0 2002-JP2779 20020322
M1 AE, AG, AL, AH, AT, AU, AZ, AA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CL, BE, DK, DH, DZ, EC, BE, ES, F1, GB, GD, GE, GH, GM, HR, HU, CL, BL, LI, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LK, LS, LT, LU, LV, MA, MD, MG, MK, MN, MM, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SS, S1, SK, SL, TJ, TM, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZM, AM, AZ, BY, KG, KZ, MD, RU, TJ,
WO 2002-JP2779
```

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

MARPAT 137:310823

This document discloses a method for preparing alkyl 7-quinolinyl-3,5-dihydroxyhept-6-enoate represented by the formula I (R represents an

group or an aryl group), characterized in that a compound represented by formula II (R is as defined above) , or a compound represented by the formula III (R is as defined above) is reduced by sodium borohydride in the presence of a boron compound represented by the formula R'OB(R'')2

(R' and R''represent independently an alkyl group), and then the resulting reaction mixture is treated with an aqueous solution of hydrogen peroxide. (E)-1

OTHER SOURCE(S):

ANSMER 14 OF 26 CA COPYRIGHT 2006 ACS on STN (Continued) (R = ethyl) was prepd. from (E)-II (R.= ethyl) by the title method. 147005-20-5107, borane complex RL: BYP (Byproduct); CPS (Chemical process); PEP (Physical, engineering

chemical process); PREP (Preparation); PROC (Process)
 (preparation of alkyl 7-quinolinyl-3,5-dihydroxyhept-6-enoate by
 stereoselective reduction of alkyl 7-quinolinyl-5-hydroxy-3-oxohept-6 enoate by sodium borohydride in presence of boron compound)
147008-20-6 CA
6-Reptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5dihydroxy-, ethyl ester, (3R,5S,6E)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry. Double bond geometry as shown.

THERE ARE 11 CITED REFERENCES AVAILABLE FOR REPERENCE COUNT: THIS

FORMAT

RECORD. ALL CITATIONS AVAILABLE IN THE RE

ANSWER 15 OF 26 CA COPYRIGHT 2006 ACS on STN (Continued)

A process for producing the title compound (I) and optically active

AB A process for producing the tractions...

with microorganism by fermentation was given. I is useful as serum cholesterol-reducing agent. Preparation of Et ester of I (3R,5S-DOLE) and its derivs. 35,5R-, 35,5S-, and 3R,5R-DOLE with Saccharomycopsis fibuligera from 5-Mol. i.e.

from 1-Mol. i.e.

from 5-Mol. i.e.

from 5-Mol. i.e.

from 1-Mol. i.e.

fr

IT 167073-18-99
RL: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(process for producing
(3R,5S)-(8]-7-(2-cyclopropyl-4-(4-fluorophenyl)quinolin-3-yl)-3,5-dihydroxyhept-6-enoic acid ester and derivs.)
RN 167073-18-9 CA
CN 6-Heptenoic acid. 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester, (3S,5R,6E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

REFERENCE COUNT: THIS

THERE ARE 15 CITED REFERENCES AVAILABLE FOR RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

Page 15

L9 ANSMER 15 OF 26
ACCESSION NUMBER:
TITLE:
17:139496 CA
Processe for producing (1R,55)-(8)-7-[2-cyclopropyl-4-(4-fluorophenyl)-quinolin-3-yl]-3,5-dihydroxyhept-6-enoic acid ester and derivatives
INVENTOR(5):
Hare, Mari; Takuma, Yuki; Katsurada, Manabu;

INVENTOR(S): Hosokawa,

Akemi; Matsumoto, Youichi; Kasuga, Yuzo; Watanabe,

Akemi; Matsumoto, Youichi; Kasuga, Yuzo; Matana Naoyuki Mitsubishi Chemical Corporation, Japan; Nissan Chemical Industries, Ltd. PCT int. Appl.. 63 pp. CODEN: PIXXO2 Patent Japanese PATENT ASSIGNEE(S):

SOURCE:

DOCUMENT TYPE: LANGUAGE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE

MO 2002063028 A1 20050815 MO 2002-JP835 20020201

N: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DB, DK, DM, DZ, EC, ER, ES, PI, GB, GD, GE, GH, GM, HR, HU, ID, UL, IN, IS, KE, RG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MD, MK, MD, MC, MC, MZ, MC, NO, MZ, CM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TM, TR, TT, TZ, UA, UG, US, UZ, VM, YU, AZ, AM, ZM

RM: GH, GM, KE, LS, MM, MZ, SD, SL, SZ, TZ, UG, ZM, ZM, AT, BE, CH, CT, DE, DK, ES, PI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BD, CF, CG, CI, CM, GA, GM, GQ, GW, ML, MR, NE, SN, TD, TG

JP 200310897 A2 20031051 JP 2002-254231 20020201

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, NC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

CN 1633502 A 20050629 CN 2002-629855 20030710

US 6965031 B2 20051115

PRIORITY APPLN. INFO: PATENT NO. KIND /DATE APPLICATION NO. JP 2001-331480 A 20011029

WO 2002-JP835

W 20020201

OTHER SOURCE(S): CASREACT 137:139496; MARPAT 137:139496

L9 ANSWER 15 OF 26 CA COPYRIGHT 2006 ACS on STN (Continued)

L9 ANSMER 16 OP 26 CA COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:

116:112193 CA

Synthesis and biological evaluations of
quinoline-based BNG-CoA reductase inhibitors

SUZUKI, M.; Ivasaki, H.; Pujikawa, Y.; Kitahara, M.;

Sakashita, M.; Sakoda, R.

CORPORATE SOURCE:

CORPORATE SOURCE:

Dioorganic & Medicinal Chemistry (2001), 9(10),
2727-2743

CODEN: BMECEP; ISSN: 0968-0896

PUBLISHER:
Elsevier Science Ltd.

DOCUMENT TYPE:

LANGUAGE:

CONTRES SOURCES

CARTAGO CONTRACT

LANGUAGE:

CONTRES SOURCES

CARTAGO CONTRACT

COUNTAI

A series of quinoline-based 3,5-dihydroxyheptenoic acid derive. were
synthesized from quinolinecarboxylic acid esters by homologation, aldol
condensation with Ex acctoacetate diamion, and reduction of
3-hydroxyketone to
evaluate their ability to inhibit the enzyme RMG-CoA reductase in vitro.
In agreement with previous literature, a strict structural requirement
exists on the external ring, and 4-fluorophenyl is the most active in

this
system. For the central ring, substitution on positions 6, 7, and 8 of

system. For the central ring, substitution on positions 6, 7, and 8 of the central quinoline nucleus moderately affected the potency, whereas

the alkyl side chain on the 2-position had a more pronounced influence on activity. Among the derivs., NK-104 (pitavastatin calcium), which has a cyclopropyl group as the alkyl side chain, showed the greatest potency. We found that further modulation and improvement in potency at inhibiting HMG-COA reductase was obtained by having the optimal substituents

flanking the desmethylmevalonic acid portion, i.e., 4-fluorophenyl and

cyclopropyl, instead of the usual iso-Pr group. IT 697216-82-5

697214-82-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis and biol. evaluations of quinoline-based HMG-CoA reductase inhibitors)
697214-82-5 CA
6-Meptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-6,7-dimethoxy-3-quinolinyl]-3,5-dihydroxy-, ethyl ester, (3R,5S,6E)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry. Double bond geometry as shown.

ANSWER 17 OF 26 CA

L9 ANSWER 17 OF 26 CA ACCESSION NUMBER: TITLE: (3R,5S,6E)-7-(substituted

COPYRIGHT 2006 ACS on STN

136:36497 CA
Manufacture of
d-quinolyl)-3,5dihydroxyhept-6-enoic acid esters by stereoselective
enzymic hydrolysis
Tokuda, Shinichiro; Okabe, Toshiyuki; Soma, Tamotsu
Nissan Chemical Industries, Ltd., Japan; Sankyo Kasei
Kogyo K. K.
Jpn. Kokai Tokkyo Koho, 7 pp.
CODEN: JKKKAP
Patent
Japanese
1

INVENTOR(S): PATENT ASSIGNEE(S):

SOURCE:

DOCUMENT TYPE: LANGUAGE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE JP 2001352996 PRIORITY APPLN. INFO.: A2 20011225 JP 2000-175316 JP 2000-175316 20000612

OTHER SOURCE(S):

MARPAT 136:36497

AB The compds. (3R,5S,6E)-I (R = C1-4 alkyl) (II), useful as intermediates for (3R,5S,6E)-7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolyl)-3,5-dihydroxyhept-6-enoic acid salts as hypolipemics and antistherosclerotics, are memufactured by treating a mixture of stereoisomers of (6E)-I including II with acylating agents in the presence of hydrolases, removing the hydrolases from the reaction mixture, and then separating II from the

ure A mixture (3.37 g) of II (R = Rt) 49.7, (38,5R,6E)-I (R = Et) 49.7, (38,5S,6E)-I (R = Et) <0.3 and (3R,5R,6E)-I (R = Et) <0.3 and (3R,5R,6E)-I (R = Et) <0.3 and treated with isopropenyl acetate and Lipase PS in Me3COMe at 40° for 94 h to give 1,40 g II (R = Et) with 99.4 a.e.

RL: PUR (Purification or recovery); PREP (Preparation)
(manufacture of optically-active quinolyldihydroxyheptenoic acid

ers from
stereoisomer mixts. using acylating agents and hydrolases)
167073-19-0 CA
6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-Page 16

ANSWER 16 OF 26 CA COPYRIGHT 2006 ACS on STN (Continued)

REFERENCE COUNT:

THERE ARE 48 CITED REFERENCES AVAILABLE FOR

RECORD. ALL CITATIONS AVAILABLE IN THE RE

PORMAT

ANSWER 17 OF 26 CA COPYRIGHT 2006 ACS on STN (Continued) dihydroxy-, ethyl ester, (3R,5S,6B)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

.9 ANSWER 18 OF 26 CA COPYRIGHT 2006 ACS on STN

.132:93197 CA

First systematic chiral syntheses of two pairs of enantiomers with 3,5-dihydroxyheptenoic acid chain, associated with a potent synthetic statin NR-104

STURNEY, Mikko; Yanagawa, Yoshinobu; Iwasaki, Hiroshi; Kanda, Hiroyasu; Yanagihara, Kazufumi, Matsumoto, Hiroo; Ohara, Yoshio; Yazaki, Yukari; Sakoda, Ryoxo

Central Research Institute, Nissan Chemical

AUTHOR(S):

CORPORATE SOURCE: Industries

Industries

Ltd., Chiba, 274-8507, Japan

SOURCE: Bioorganic 4 Medicinal Chemistry Letters (1999),
9(20), 2977-2982

CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Blaevier Science Ltd.

DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 132:93197

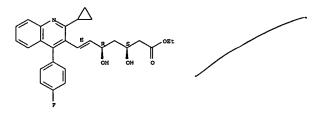
AB All 4 enantiomers of the synthetic statin NK-104 were prepared The synthetic statin NK-104 were prepared to synthetic statin NK-104 were synthetic statin NK-104 were synthetic statin NK-104 were synthetic statin NK-104 were

isomers (NK-104 and its enantiomer) were obtained efficiently by diastereomer resolution. The anti-diol isomers (3-epimer and 5-epimer)

prepared effectively by asym. aldol reaction followed by anti attreoselective reduction as key steps. Their purity detns. were effected by chiral HPLC anal.

IT 147008-20-69
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of the enantiomers of NK-104)
RN 147008-20-6 CA
6-Heptenoic acid, 7-(2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester, (3R,5S,6E)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry. Double bond geometry as shown.



REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR

L9 ANSWER 19 OF 26 CA COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:
TITLE:
125:58345 CA
Preparation of optically active
quinolyldihydroxyheptenoates as intermediates for
anticholesteremics
Harada, Katsumeas; Matsushita, Akio; Sasaki, Hiroshi;
Kawachi, Yasuhiro
Ube Industries, Ltd., Japan; Ube Kosan KK; Nissan
Chemical Industries Ltd.
Jon. Kokai Tokkyo Koho, 9 pp.
COUNENT TYPE:
LANGUAGE:
PANILY ACC. NUM. COUNT:
1 Japanese
1 Japanese
1 ATENT INFORMATION:

PAMILY ACC. NUM. COUNT: PATENT INFORMATION:

DATE PATENT NO. KIND APPLICATION NO. JP 08092217 JP 3554036 PRIORITY APPLN. INFO.: 19960409 20040811 19940906

OTHER SOURCE(S): CASREACT 125:58345; MARPAT 125:58345

СНСН (ОН) СН<sub>2</sub>ХСН<sub>2</sub>СО<sub>2</sub>R6 R4R3C (OH) CHR2N: CH

The title compds. I (R6 = alkyl, Ph; X = CHOH) are prepared by reaction (E)-3-{2-cyclopropyl-4-(4-fluorophenyl)quinolin-3-yl)prop-2-en-1-el (III) with diketene in organic solvents in the presence of Ti complexes,

prepared
 from optically active Schiff bases II (R1 = alkyl; R2 = H, alkyl; Ph; R3,
 R4 = H, alkyl; R2 = R3 = R4 = H; n = 0-4) and Ti(OR5)4 (R5 = alkyl;
 Ph), followed by syn-reduction of the optically active I (X = CO). III

diketene were added to a mixture of (S)-II (R1 = 3-CMe3, R2 = CHMe2,

Page 17

L9 ANSWER 18 OF 26 CA COPYRIGHT 2006 ACS on STN (Continued)
RECORD. ALL CITATIONS AVAILABLE IN THE RE PORMAT

ANSWER 19 OF 26 CA COPYRIGHT 2006 ACS on STN (Continued)
H) and Ti(OEt)4 in CH2Cl2 and stirred at -50° for 62 h to give 72<sup>h</sup>
(55)-(E)-I (R6 = Et, X = CO) with 78<sup>h</sup> ee, redn. of which with NaBH4 and
Me2BOMe in THF-MeOH at -75° for 3.5 h gave 88<sup>h</sup> (3R,55)-(E)-I (R6 =
Et, X = CHOH) (IV). IV was converted into
(65)-(E)-6-[2-cyclopropyl-4(4-fluorophenyl)quinolin-3-ylethenyl)-4-hydroxy-3,4,5,6-tetrahydro-2Hpyran-2-one in 89<sup>h</sup> yield and 78<sup>h</sup> ee.
187073-19-0P

IT 147073-19-09 RL: IMP (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation of optically active quinolyldihydroxyheptenostes from quinolylpropenal and diketene by addition with Ti complexes and reduction)
RN 167073-19-0 CA

ction)
167073-19-0 CA
6-Heptenoic acid, 7-[2-cyclopropyl-4-[4-fluorophenyl]-3-quinolinyl]-3,5dihydroxy-, ethyl ester, (3R,5S,6E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

.9 ANSMER 20 0P 26 CA COPYRIGHT 2006 ACS on STN

LOCESSION NUMBER:
114:141135 CA
Preparation of quinolineldehyde derivative as
intermediate for quinoline type mevalonolactomes
(INVENTOR(S): Randa, Hirroyasu; Obara, Yoshio;
1Reda, Hirrokasu; Murakami, Tatsufumi
Daicel Ragaku Kogyo KK, Japan; Niesan Kagaku Kogyo KK
Jpn. Kokai Tokkyo Koho, 10 pp.

COURENT TYPE:
ANCIUMGE: JKXXAF
Patent
ANCIUMGE: JAPANEE CALLER J INVENTOR(S): PATENT ASSIGNEE(S): SOURCE: DOCUMENT TYPE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION: PATENT NO. KIND APPLICATION NO.

DATE DATE JP 08003138 JP 3739432 PRIORITY APPLN. INFO.: 19960109 JP 1995-35587 19950223 JP 1994-28596 A 19940225

OTHER SOURCE(S): MARPAT 124:343135

AB The title compound I is prepared by reaction of olefin II [2 = Q1, etc.] with

ozone. Thus, a mixture of ozone and oxygen was introduced into II {Z =

in ethanol and methanol at -60 to -72° during 1.5 h.
Dimethylsulfide was then added to the reaction mixture at -72°; and
the resulting mixture was warmed to room temperature during 1 h to give,

L9 ANSMER 21 OF 26 CA COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 124:86587 CA
TITLE: Process for producing optically active aromatic mevalionolactone compounds
INVENTOR(s): Ikeda, Hirokazu; Murakami, Tatsushi; Matsumoto, INVENTOR(S):

Chara, Yoshio; Kanda, Hiroyashu
Daicel Chemical Industries, Ltd., Japan; Nissan
Chemical Industries, Ltd.
PCT Int. Appl., 31 pp.
CODEN: PIXXD2
Patent
Japanese
1 PATENT ASSIGNEE(S):

SOURCE:

DOCUMENT TYPE: LANGUAGE: FAMILY ACC. NUM. COUNT: PATENT INPORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE

A mevalonolactone compound is produced by batchwise chromatog. or pseudo-moving bed method both using a column filled with a packing material for optical resolution comprising a polysaccharide derivative

pseudo-moving bed method comprises jointing endlessly a number of

columns to
form a circulating flow path wherein a fluid is forcibly circulated in

direction, providing alternately along the direction of flow of the circulated fluid inlets for feeding the fluid into the column and outlets for drawing the fluid out of the column, moving intermittently the positions of the inlets and the outlets in the direction of flow of the circulated fluid, feeding a solution containing a racemate of a lonplactone.

mevalonolactone compound and an eluent into a circulating path through the inlets, and drawing out simultaneously a solution enriched with nonadsorbates and a

tion enriched with adsorbates through the outlets. 172336-33-3

172336-33-3
RL: ANT (Analyte); ANST (Analytical study)
(process for producing optically active mevalonolactone compound)
172336-33-3
CA
6-Heptenoic acid, 7-{2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-

L9 ANSWER 20 OF 26 CA COPYRIGHT 2006 ACS on STN (Continued)

workup, 29% I. 167073-18-99 17

RL: PUR (Purification or recovery); PREP (Preparation) (preparation of quinolinaldehyde derivative as intermediate for quinoline type mevalonolactones)

move/conservations:
157073-18-9 CA
6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl}-3,5-dihydroxy-, ethyl ester, (3S,5R,6E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

ANSWER 21 OF 26 CA COPYRIGHT 2006 ACS on STN (Continue dihydroxy-, ethyl ester,  $[R-(R^*,S^*)]-(9CI)$  (CA INDEX NAME) (Continued)

Absolute stereochemistry. Rotation (-). Double bond geometry unknown.

L9 ANSMER 22 OF 26
ACCESSION NUMBER:
131:168993 CA
Optically active \$\textit{B}\$-aminoalkoxyborane complex as asymmetric reducing agent
INVENTOR(S):
RASHIMARS, Hiroshi; Suzuki, Mikio; Ohara, Yoshio
Nissan Chemical Industries Ltd., Japan
PCT Int. Appl., 91 pp.
CODE: PIXXD2

DOCUMENT TYPE:
LANGUAGE:
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PATENT INPORMATION:

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	US	5786	485					1998	0728		US	19	97-	8481	172 169 174 5			13	970	129
	US	5808	098					1998	0915		US	19	97-	8481	69			15	970	129
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OTHER SOURCE(S):

CASREACT 123:168993; MARPAT 123:168993

L9 ANSWER 22 OF 26 CA COPYRIGHT 2006 ACS on STN (Continued)

L9 ANSWER 22 OF 26 CA COPYRIGHT 2006 ACS on STN (Continued)

. STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT .

Optically active  $\beta$ -minoslkoxyborane complexes are disclosed, specifically I (R1 = C1-C8 alkyl, C1-C7 cycloslkyl, C7-C11 aralkyl or C6-C10 aryl; R3 = H, C1-C8 alkyl, C3-C7 cycloslkyl or C7-C11 aralkyl; or R1R3 = (CH2)n wherein n = 3 or 4; Ar = naphthyl, anthryl or phenanthryl, which may be substituted by 1-3 substituents selected from halo, nitro, C1-C6 alkyl, C3-C7 cycloslkyl, C3-C6 alkenyl or alkynyl, C7-C11 aralkyl, C6-C10 aryl, C1-C6 alkoxy, and styrene polymer substituents). The complexes are useful for reducing carbonyl compda to optically active alcs., and especially for reducing 1,3-dicarbonyl compds. to optically ve

alcs., and especially to recording ...

1,3-syn-diols. For example, reduction of proline Et ester with LiAlH4 to give

(\$)-prolinol, cyclocondensation of this with β-naphthaldehyde to give an oxazolidine derivative (quant.), reduction of this with NaEH4 to give

an oxaxolidane derivative (quest.), and anino
alc. (quant.), and reaction of the latter with BH3.THF (quant.), gave the
(S)-isomeric complex II. Reduction of diketo ester III using II and

(S)-isomeric complex II. Reduction of diketo ester III using II and ELIBOME
in THF at 20° gave the (38,5R)-syn-diol IV in 53% yield and 100% enantiomeric excess (ee). In contrast, several similar known borane complexes gave 28-78% yield but only 6-23% ee.

II 167073-18-99, (38,5R,E)-Ethyl 7-[2-cyclopropyl-4-(p-fluorophenyl)quinolin-3-yl]-3,5-dihydroxy-6-heptenoate RL: IMF (Industrial manufacture); SFM (Synthetic preparation); PREP (Preparation) (reduction product; preparation of optically active β-mminoalkoxyborane complexes for asym. reduction of (di)carbonyl compds.)

RN 167073-18-9 CSA
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester, (38,5R,6E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

L9 ANSWER 23 OF 26 CA	COPY	RIGHT 2006 A	CS on STN	
ACCESSION NUMBER:	119:1	17112 CA		
TITLE:	Prepa:	ration of (h	eterocyclylvinyl)mevalo	nic lactor
	analo	as as antiat	herosclerotics	
INVENTOR(S):	Saito	. Yasushi: R	Litahara, Masaki; Sakash	ita.
Mitsuaki:				
	Toyod	a. Kvomi: Sh	ibazaki, Toshie	
PATENT ASSIGNEE(S):			ndustries, Ltd., Japan;	Kowa Co
***************************************	Ltd.		,,	
SOURCE:		Pat. Appl.,	64 PD	
		: EPXXDW	<b></b> -	
DOCUMENT TYPE:	Paten			
LANGUAGE:	Engli			
PAMILY ACC. NUM. COUNT:	1	•••		
PATENT INFORMATION:	•			
PAILMI INFORMATION:				
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 535548	A1	19930407	EP 1992-116417	19920924

PATENT NO.	KIND DATE	APPLICATION NO.	DATE
EP 535548	A1 19930407	EP 1992-116417	19920924
BP 535548	B1 20011121		
R: AT, BE, CH,	DE, DK, PR, GB,	IE, IT, LI, LU, NL, SE	
JP 06329540	A2 19941129	JP 1991-257870	19911004
JP 3130342	B2 20010131		
AT 209035	B 20011215	AT 1992-116417	19920924
AU 9226012	A1 19930408	AU 1992-26012	19920928
AU 652669	B2 19940901		
NZ 244555	A 20000623	NZ 1992-244555	19920930
US 6162798	A 20001219	US 1992-953716	19920930
NO 9203858	A 19930405	NO 1992-3858	19921002
NO 302452	B1 19980309		
CA 2079706	AA 19930415	CA 1992-2079706	19921002
CA 2079706	C 20040330		
HU 62794	A2 19930628	HU 1992-3138	19921002
HU 214624	B 19980428		
CZ 281786	B6 19970115	CZ 1992-3027	19921002
RU 2114620	C1 19980710	RU 1992-5052949	19921002
SK 279277	B6 19980909		19921002
PRIORITY APPLN. INFO.:		JP 1991-257870 A	19911004

OTHER SOURCE(S): MARPAT 119:117112

L9 ANSWER 23 OF 26 CA COPYRIGHT 2006 ACS on STN (Continued)

Title compds. {I; R = substituted-Ph; RJ = H, (cyclo)alkyl, (cyclo)alkenyl, (substituted)Ph, etc.; R4R5 = atoms to complete a fused benzene or 5- or 6-membered heteroaryl ring; Y = CH2, CH2CH2, CH:CH,

ctc.;

2 = 4-hydroxy-2-oxo- or 2,4-dioxo-6-tetrahydropyranyl, QCH2MCH2CO2R12, etc.;

2 = 4-hydroxy-2-oxo- or 2,4-dioxo-6-tetrahydropyranyl, QCH2MCH2CO2R12, etc.; Q = CO, CH(OM), etc.; R12 = H, ammonium, physiol. labile ester residue, etc.; M = CO, CH(OM), etc.], inhibitors of atherosclerotic intimal thickening, were prepared Thus, thienopyridinecerboxyaldehyde II (R6 = CHO) was condensed with BuSAnc(OEt): CH2 and the product hydrolyzed to give II (R6 = (E)-CH:CHCHO) which was condensed with MeCOCH2CO2Et to give, in 3 addnl. steps, II (R6 = oxopyranylvinyl group Q). The latter gave 100% inhibition of smooth muscle cell proliferation at 10-6 M (intimal) and 10-5 M (medial) in vitro.

IT 131661-13-0 PR: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or resgent)

(preparation and reaction of, in preparation of antiatherosclerotic)

RN 121661-13-0 CA

CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester (9CI) (CA INDEX NAME)

L9 ANSMER 24 OF 26 CA COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 118:233897 CA
TITLE: Preparation of disatereomer salt of optically active
quinolinemevalonic acid
Ohara, Yoshio, Suzuki, Mikio; Yanagawa, Yoshinobu;
Iwaski, Hiroshi; Miyachi, Nobuhide
PATENT ASSIGNEE(S): Nissan Chemical Industries, Ltd., Japan
SOURCE: CODEN: EFXXDM
DOCUMENT TYPE: Patent
LANGUAGE: PALLING English
PAMILY ACC. NUM. COUNT: 1

FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

PATENT NO.	KIND DATE	APPLICATION NO.	DATE
***************************************			
EP 520406 EP 520406	A1 19921230	EP 1992-110636	19920624
EP 520406	B1 19980902		
R: AT, BE, CH,	DE, DK, ES, FR, GE	GR, IT, LI, LU, MC	, NL, PT, SE
JP 05148237	A2 19930615	JP 1992-127277	19920520
JP 3528186	B2 20040517		
CA 2072162	AA 19921225	CA 1992-2072162	19920623
CA 2072162	C 20021119		
US 5284953	A 19940208	US 1992-902863	19920623
EP 742209	A2 19961113	EP 1996-107815	19920624
EP 742209	A3 19970514		
R: AT, BE, CH,	DE, DK, ES, FR, GE	B, GR, IT, LI, LU, MC	, NL, PT, SE
AT 170513	B 19980915	AT 1992-110636	19920624
AT 170513 ES 2120973	T3 19981116	ES 1992-110636	19920624
KR 208867	B1 19990715	KR 1992-11018	19920624
US 5473075	A 19951205	US 1993-123117	19930920
US 5514804	A 19960507	US 1995-450383	19950525
US 5514804 PRIORITY APPLN. INFO.:		JP 1991-151810	A 19910624
		US 1992-902863	
		EP 1992-110636	A3 19920624
		US 1993-123117	A3 19930920

: сисиси³сиси³со³н А. А.

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ANSWER 23 OF 26 CA COPYRIGHT 2006 ACS on STN (Continued)

L9 ANSWER 24 OF 26 CA COPYRIGHT 2006 ACS on STN (Continued)

AB A disstereomer salt of the title compound (I) which is an intermediate for

preparation of optically active quinolinemevalonic acid derivs. with

n. biol. activity is prepared by resolution of its racemic parent. Et  $\{\pm\}$  -  $\{\pm\}$  -

IT

give the (E)-(3R,5S)-I.
147008-30-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(asponification of)
147008-30-6
CA
6-Heptenoic acid, 7-(2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5dihydroxy-, ethyl ester, (3R,5S,6E)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.

L9 ANSWER 25 OF 26 CA COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 114:82195 CA 14:82195 CA

PANILY ACC. NUM. COUNT: PATENT INFORMATION:

PATENT NO. DATE APPLICATION NO. KIND DATE DE 3905908 PRIORITY APPLN. INFO.: DE 1989-3905908 DE 1989-3905908 A1 19900906 19890225

OTHER SOURCE(S):

CASREACT 114:82195; MARPAT 114:82195

The title compds. (I;  $A = \{un\}$  substituted heterocyclyl, aryl, alkyl; B = cycloslkyl,  $\{un\}$  substituted alkyl, aryl; D = H, alkyl; E, F, G = H, halo, alkyl;  $R = CH(OH) CH2CH(OH) CH2CO2R2 or <math>\delta$ -lactone form thereof; R1 = H, alkyl; R2 = H, alkyl, aryl, cation; X = CH2CH2. CH:CH) were prepared Thus, 2-amino-4'-fluoro-3-methylbenzophenone (preparation given) was cyclocondeneed with R3COCH2CO2Me (R3 = cyclopropyl) to give quinolinecarboxylate II (A = 4-FC6H4)(III; R4 = CO2Me) which was acted

quinoinecaroxylate ii (A = 4-Y.ChH) (iii; ka = U.Zhe) which was 'exted in 2 steps to III (R4 = CHO). The latter was condensed with (EtO)2P(O)CH:CHNHRS (R5 = cyclohexyl) and the product [III; (B)-CH:CHCHO] condensed with MeCOCH2CO2Me to give, after reduction, III (R4 = (B)-CH:CKH(HO)HCH2CH(HO)HCH2CO2Me) which was 53 times as potent as mevinolin in inhibition of 3-hydroxy-3-methylglutaryl-CoA (HMG-COA) reductase in vitro. 131775-33-2 RL: RAC (Riological activity or effector, except adverse): BSU

RL: BAC (Biological activity or effector, except adverse); BSU (Biological

logical study, unclassified); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent) (HMG-COA reductase inhibitor activity of) 131775-33-2 CA 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-6,8-dimethyl-3-

L9 ANSWER 26 OF 26 CA COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:

TITLE:

Quinolinylheptenoic acid derivatives as anticholesteremics, their preparation, and formulations containing them
Pujikwa, Yoshihiro; Suzuki, Mikio; Iwasaki, Hiroshi; Sakashita, Mitsuaki; Kitahara, Masaki

PATENT ASSIGNER(S):

SOURCE:

DOCUMENT TYPE:

LANGUAGE:

PAHLLY ACC. NUM. COUNT:

English
English
English
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English

PATENT INFORMATION:	•			
PATENT NO.	KIND DA	TE P	APPLICATION NO.	DATE
EP 304063	A2 19	890222 E	P 1988-113448	19880818
EP 304063				
EP 304063	B1 19	941130		
			IT, LI, LU, NL, SE	
			P 1988-193606	
JP 01279866 JP 2569746	B2 19	970108		
CA 1336714	A1 19	950815	A 1988-574999	19880817
ES 2067460	T3 19	950401 E	S 1988-113448	19880818
US 5011930	A 19	910430 L	IS 1990-483720	19900223
US 5011930 US 5102888 US 5185328 US 5872130	A 19	920407 L	IS 1990-483724	19900223
US 5185328	A 19	930209 L	S 1990-483829	19900223
US 5872130	A 19	990216 L	IS 1990-631092	19901219
US 5856336	A 19	990105 L	IS 1992-883398	19920515
US 5854259 PRIORITY APPLN. INFO.:	A 19	981229 U	IS 1992-978884	19921119
PRIORITY APPLN. INFO.:		3	IP 1987-207224	A 19870820
		a	P 1988-15585	A 19880126
		a	P 1988-193606	A 19880803
		υ	IS 1988-233752	A3 19880819
		υ	IS 1990-631092	A3 19901219
		υ	JS 1992-883398	A3 19920515

OTHER SOURCE(S):

R SOURCE(S): MARPAT 111:134010

For diagram(s), see printed CA Issue.

The title compds. I [R1-R4, R6 = H, C1-6 alkyl, C3-6 cycloalkyl, C1-3 alkoxy, etc.; or R1 and R2, R3 and R4 may form CH:CHCH:CH, etc.; Y = CH2, CH2CH2, CH:CH, CH2CH:CH, CH:CHCH2; Z = QCH2MCH2CO2R12, Q1, etc.; Q =

C(0),

CH(OH), etc.; W = C(0), C(R11) (OH), etc.; R11 = H, C1-6 alkyl; R12 = H,
R14; R14 = physiol. hydrolyzable alkyl, M; M = NH4, Na, K, etc.; R5 = H,
C1-6 alkyl, C2-3 alkenyl, C3-6 cycloalkyl, etc.], useful as cholesterol
biosynthesis inhibitors, were prepared Reduction of Et (E3-7-[4'-(4'fluorophenyl)-2'-(1'''-methylethyl)quinolin-3'-yl]-5-hydroxy-3-oxohept-6enoate (preparation given) with NaBH4, followed by saponification in
0.5N NaOH, gave

(E)-3,5-dihydroxy-7-[4'-{4''-fluorophenyl}-2'-{1'''-methylethyl}-quinolin-3'-yl]-hept-6-enoic acid Na salt (II). II exhibited an IC50 of 1.0 + 10-8M against cholesterol biosynthesis from acetate in vitro. A

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ANSWER 25 OF 26 CA COPYRIGHT 2006 ACS on STN (Continued) quinolinyl]-3,5-dibydroxy-, methyl ester, [R\*.5\*-(E)]- (9CI) (CA INDEX

Relative stereochemistry.
Double bond geometry as shown.

ANSWER 26 OF 26 CA COPYRIGHT 2006 ACS on STN (Continued) capsule formulation contg. II 1, lactose 3.5, cellulose 10, Mg stearste 0.5 g is given. 122661-13-0P

121661-13-09
RE: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as cholesterol biosynthesis inhibitor)
121661-13-0 CA
6-Heptenoic acid, 7-[2-cyclopropyl-4-[4-fluorophenyl]-3-quinolinyl]-3,5-dihydroxy-, ethyl ester (9CI) (CA INDEX NAME)

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(FILE 'HOME' ENTERED AT 14:33:52 ON 08 MAR 2006)

FILE 'REGISTRY' ENTERED AT 14:34:02 ON 08 MAR 2006

L1 STRUCTURE UPLOADED

L2 2 S L1 SAM

L3 24 S L1 FULL

FILE 'CA' ENTERED AT 14:34:31 ON 08 MAR 2006

L4 32 S L3

L5 83200 S LIQUID CHROMATOGRAPH?

L6 4 S L4 AND L5

L7 3 S L4 AND RESOLV?

L8 6 S L6 OR L7 L9 26 S L4 NOT L8

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---Logging off of STN---

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Executing the logoff script...

=> LOG Y

STN INTERNATIONAL LOGOFF AT 14:35:46 ON 08 MAR 2006